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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,169	04/20/2007	Toshiaki Tagawa	701018	1668

23460 7590 02/26/2010

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EXAMINER	
HUFF, SHEELA JITENDRA	
ART UNIT	PAPER NUMBER
1643	

NOTIFICATION DATE	DELIVERY MODE
02/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/581,169	TAGAWA ET AL.	
	Examiner	Art Unit	
	Sheela J. Huff	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 October 2009 and 26 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22,23,25,26 and 28-64* is/are pending in the application.

4a) Of the above claim(s) *25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-23 and 28-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/29/09 has been entered.

The supplemental amendment filed 1/26/10 has also been entered.

Claims 22-23, 25-26 and 28-64 are pending.

Claims 25-26 are withdrawn from consideration as being drawn to a non-elected invention.

Claims 22-23 and 28-64 are currently under consideration.

All pending rejections are withdraw in view of applicant's amendment.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

Claims 28 and 47-64 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION.

In claim 28 the liposome is composed of triglycerol and chloesterol. However, on page 9, lines 23-25, of the specification the cholesterol must be used in combination with

phospholipids. The specification does not provide support for liposomes solely containing triglycerol and chloesterol.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 22-23, 28-32, 34-50 and 52-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slater et al US 2003/0133973 in view of Modi US 6193997.

Slater et al disclose liposomes which have hydrophilic polymer chains on the outside of liposomes and the polymer can be polyethylene glycol (0064-0067). The liposomes are compsed of phosplipids and cholesterol ([0024]). The reference also discloses agents (includes compounds of MW 400-2,000,000 daltons and polyanionc polymers entrapped in the liposomes and these include sulfate polysaccharies, hyaluronic acid, chrondotin sulfate, celluloses and cellulose derivatives (0093-0094). The size of the liposomes are 40nm-250nm ([0081]). These liposomes are used for entrapment of water-soluble compounds ([0079]).

The only difference between the reference and the instant invention is the scope of water soluble substances and the use of a triglycerol in the lipsome.

Modi discloses mixed liposome pharmaceutical formulations comprising a proteinic pharmaceutical agent, water, at least one membrane-mimetic amphiphile and at least one phospholipid wherein the phospholipid can be phospholipid GLA (glycolic, lactic acid) and/or triolein (reads on applicant's triglycerol) (see col. 3, lines 30-65). The proteinic pharmaceutical agent can be monoclonal and polyclonal antibodies (reads on ligands of claims 12-15), chemotherapeutic agents and other non proteinaceous compounds such as anitsense oligos and RNA (see col. 5, lines 5-20). Modi also clearly shows that many different phospholipids can be used in making the lipsomes and that all them are within the purview of one skilled in the art.

In view of the known fact that liposomes can contain triolein and since it is within the purview of one skilled in the art to use any of the known phospholipids of Modi, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use triolein

in the liposome composition. The entrapment of other agents (water soluble substances) such as proteins, antisense oligos etc is obvious in view of Modi.

Claims 22-23 are product-by-process claims and when evaluating compound claims the process carries little weight. Specifically, the process steps are only considered to the extent that they impart distinctive structural characteristics to the final product. In the instant case, the use of phospholipid, triglycerol and cholesterol impart distinctive structural characteristics to the final product.

While the reference is silent as to the encapsulation rate of the compound in the internal cavity, it is an expected feature that the encapsulation rate of the reference is the same as that of the claimed invention. Since the Patent and Trademark Office does not have the facilities for examining and comparing the claimed encapsulation rate with that of the reference, the burden of proof is upon the Applicants to show a distinction between the rates. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 197) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.).

Response to Applicant's arguments

Applicant argues that the process of making the liposome results in the particle size of the liposome being greater that the particle size of the W/O emulsion in every case and provides a declaration and reference to support this. The fact that the process of making the liposome may be novel, does not change the structure of the final product. The final product in the instant claims is a liposome containing phosphoipid, triglyerol and cholesterol with the particle size being 300nm or less. And these limitations are met by the combination of the references.

Applicant argues unexpected results in that the combination of the triglycerol and cholesterol impart an improved thermodynamic stability of the membrane of the liposome which results in a high rate of encapsulation. Applicant relies on Example 7 and Figures 2A and 2B for support. The data presented in the example/figures is for liposomes with a particle size of less than 200nm (whereas the particle size in the claims is 300nm or less) and only discloses the encapsulation rate of CF (whereas in the claims any water-soluble substance can be encapsulated). Additionally, it is not clear what controls, if any, were used. Thus, the data presented in not commensurate in scope of the claims. Furthermore, a proper comparison for unexpected results is a comparison between the closest prior art and applicant's invention. No such comparison is present.

Claims 22-23 and 28-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slater et al US 2003/0133973 in view of Modi US 6193997, EP 1170018 and applicant's admission on page 6 of the specification. The rejection is re-written in view of the addition of claims 22-24.

Slater et al and Modi have been discussed above.

The combination of the references does not disclose the compounds of claims 33 or 51 or a ligand bound to the surface of the liposome.

The EP reference discloses ligand bonded complexes wherein the ligand (such as an antibody directed against a tumor) is bonded thru a water-soluble macromolecule such as polyethylene glycol, polyglycolic acid, polylactic acid, polyvinylpyrrolidone and/or polyalkylene glycol to a liposome wherein the liposome encapsulates an active medicament (col. 2, lines 20-

58 and col. 5, lines 25-38). The size of liposomes are about 20-500nm (col. 6, line 10). A variety of different drugs can be encapsulated into the liposome and they include cisplatin and a variety of other anti-tumor agents.

On page 6 of the specification applicant admits that cisplatin, carboplatin, nedaplatin, gemcitabine and Ara-C are anti-tumor agents.

In view of Modi which dislcoses the incorporation of chemotherapetuic agents into the liposomes, and since both applicant and the EP reference disclose cisplatin as such an agent and since applicant admits that cisplatin, carboplatin, nedaplatin, gemcitabine and Ara-C are anti-tumor agents, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to incorporation any of the known anti-tumor agents into the liposomes of Modi with the expected benefit of treating cancer. Furthermore, in view of the EP reference it also would have been obvious to attach the antibody to the outside of the liposome thru a polyethylene glycol with the added benefit of specifically targeting the tumor.

Claims 22-23 are product-by-process claims and when evaluating compound claims the process carries little weight. Specifically, the process steps are only considered to the extent that they impart distinctive structural characteristics to the final product. In the instant case, the use of phospholipid, triglycerol and cholesterol impart distinctive structural characteristics to the final product.

Response to Applicant's arguments

Applicant's arguments have been addressed above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J. Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Monday-Thursday 6am to 2pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sheela J Huff/
Primary Examiner
Art Unit 1643

sjh